Dietary vitamin D intake and risk of type 2 diabetes in the European Prospective Investigation into Cancer and Nutrition: the EPIC-InterAct study

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Abstract: Background/Objectives:Prospective cohort studies have indicated that serum vitamin D levels are inversely related to risk of type 2 diabetes. However, such studies cannot determine the source of vitamin D. Therefore, we examined the association of dietary vitamin D intake with incident type 2 diabetes within the European Prospective Investigation into Cancer and Nutrition (EPIC)-InterAct study in a heterogeneous European population including eight countries with large geographical variation.Subjects/Methods:Using a case-cohort design, 11 245 incident cases of type 2 diabetes and a representative subcohort (N=15 798) were included in the analyses. Hazard ratios (HR) and 95% confidence intervals (CIs) for type 2 diabetes were calculated using a Prentice-weighted Cox regression adjusted for potential confounders. Twenty-four-hour diet-recall data from a subsample (N=2347) were used to calibrate habitual intake data derived from dietary questionnaires.Results:Median follow-up time was 10.8 years. Dietary vitamin D intake was not significantly associated with the risk of type 2 diabetes. HR and 95% CIs for the highest compared to the lowest quintile of uncalibrated vitamin D intake was 1.09 (0.97-1.22) (Ptrend=0.17). No associations were observed in a sex-specific analysis. The overall pooled effect (HR (95% CI)) using the continuous calibrated variable was 1.00 (0.97-1.03) per increase of 1 g/day dietary vitamin D.Conclusions:This observational study does not support an association between higher dietary vitamin D intake and type 2 diabetes incidence. This result has to be interpreted in light of the limited contribution of dietary vitamin D on the overall vitamin D status of a person.European Journal of Clinical Nutrition advance online publication, 20 November 2013; doi:10.1038/ejcn.2013.235.

DOI: https://doi.org/10.1038/ejcn.2013.235

Khaw, K T; Kühn, T; Mattiello, A; Molina-Montes, E; Nilsson, P M; Overvad, K; Quirós, J R; Rolandsson, O; Sacerdote, C; Saieva, C; Slimani, N; Sluijs, I; Spijkerman, A M W; Tjonneland, A; Tumino, R; van der A, D L; Zamora-Ros, R; Sharp, S J; Langenberg, C; Forouhi, N G; Riboli, E; Wareham, N J (2014). Dietary vitamin D intake and risk of type 2 diabetes in the European Prospective Investigation into Cancer and Nutrition: the EPIC-InterAct study. European Journal of Clinical Nutrition, 68(2):196-202. DOI: https://doi.org/10.1038/ejcn.2013.235

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Running title:

Vitamin D and type 2 diabetes risk in the EPIC-InterAct study

Abstract

Background: Prospective cohort studies have indicated that serum vitamin D levels are inversely related to risk of type 2 diabetes. However, such studies cannot determine the source of vitamin D. Therefore, we examined the association of dietary vitamin D intake with incident type 2 diabetes within the European Prospective Investigation into Cancer and Nutrition (EPIC)-InterAct study in a heterogeneous European population including 8 countries with large geographical variation.

Methods: Using a case-cohort design, 11,245 incident cases of type 2 diabetes and a representative subcohort (N=15,798) were included in the analyses. Hazard ratios (HR) and 95% confidence intervals (CIs) for type 2 diabetes were calculated using a Prentice-weighted Cox regression adjusted for potential confounders. 24-h diet recall data from a subsample (N=2347) were used to calibrate habitual intake data derived from dietary questionnaires.

Results: Median follow-up time was 10.8 years. Dietary vitamin D intake was not significantly associated with the risk of type 2 diabetes. HR and 95 % CIs for the highest compared to the lowest quintile of uncalibrated vitamin D intake was 1.09 (0.97-1.22), (p_{trend}=0.17). No associations were observed in a sex-specific analysis. The overall pooled effect [HR (95% CI)] using the continuous calibrated variable was 1.00 (0.97-1.03) per increase of 1 µg/day dietary vitamin D.

Conclusion: This observational study does not support an association between higher dietary vitamin D intake and type-2 diabetes incidence. This result has to be interpreted in light of the limited contribution of dietary vitamin D on the overall vitamin D status of a person.

Keywords: vitamin D, type-2 diabetes, dietary intake, observational study, EPIC

Introduction

Besides the 'classical' function of vitamin D in calcium homeostasis, additional biological effects of vitamin D on diabetes-related outcomes have been identified. The results of experimental cell, animal and human studies support a role of vitamin D in the prevention of type 2 diabetes.[1-4] However, the mechanisms by which vitamin D may affect type 2 diabetes risk are not fully understood. Effects of vitamin D on insulin secretion, insulin sensitivity as well as on inflammatory and autoimmune conditions associated with diabetic conditions are reported.[4-9]

Evidence from prospective observational studies for an inverse association between vitamin D status, as characterized by serum 25-hydroxyvitamin D [25(OH)D] measurements, and type 2 diabetes is strong.[10-12] After combining the data from nine prospective studies that measured serum 25(OH)D, participants in the highest (versus lowest) quartile of 25(OH)D showed a 41% (95% CI, 33%, 48%) lower risk of type-2 diabetes though any causal inference of this association remains unconfirmed.[13] Moreover, a recent metaanalysis combining results from 14 observational studies reported a significant inverse association for circulating 25(OH)D but not for dietary vitamin D.[14] Serum 25(OH)D concentration, the accepted biomarker of vitamin D status, reflects both the endogenous synthesis in the skin (following UVB exposure) and the dietary intake of vitamin D. Though in general the contribution of dietary vitamin D to the overall vitamin D status is of minor importance as compared to the endogenous synthesis of vitamin D, intra- and inter-subject variation in UVB exposure can be high, and the importance of vitamin D from diet substantially increases in situations with limited UVB exposure. Thus, analyses on the impact of dietary vitamin D and diabetes risk are meaningful. Mitri and colleagues combined data from three cohort studies and found a borderline significant inverse association between vitamin D intake >500 U/d (12.5 µg/d) and type 2 diabetes incidence (versus subjects with a vitamin D intake < 200 U/d (5 µg/d)); the

relative risk was 0.87 (95% CI, 0.76-0.99).[11] However, only one out of three cohort studies reported a significant inverse association.[15-17]

Due to its large sample size, the InterAct project within the European Prospective Investigation into Cancer and Nutrition (EPIC) provides the opportunity to investigate the association between the incidence of type 2 diabetes and dietary vitamin D prospectively in both men and women. Furthermore, the study allows a relatively wide range of dietary intake levels since data from different European countries are included.

Material and Methods

Study design and population

EPIC is a multi-centre prospective cohort study conducted since 1992 in 10 European countries.[18] In the present EPIC-InterAct study, a nested case-cohort design within 8 of the 10 countries contributing to the EPIC cohort was used.[19] The current analysis is based on data from EPIC participants in Denmark, France, Germany, Italy, the Netherlands, Spain, Sweden, and the United Kingdom (UK).

Following the case-cohort design, the study population consisted of a random baseline sample of 16.154 participants (subcohort) and 12.403 incident cases of type 2 diabetes (including 778 from the subcohort), i.e. all participants of the entire cohort with a first diagnosis of type 2 diabetes between recruitment and December 31, 2007.[19]

The final study sample after excluding participants without dietary information (N=736) consisted of 27,043 participants, including 15,798 members of the subcohort and 11,994 incident diabetes cases (including 749 cases from the subcohort).

Dietary assessment

Diet over the previous twelve months was assessed using dietary assessment instruments that were specifically developed for each participating country.[18] The questions were structured by

common food groups except for the questionnaires used in Italy and Spain, where questions were structured by country-specific meals.

All participants were asked to report their average consumption of each food by structured categories ranging from never or less than once per month to six or more times per day. In Germany, Italy, The Netherlands and Spain individual average portions were estimated, whereas standard portions were assigned to the participants in Denmark, the United Kingdom and Umeå, Sweden. A combination of methods for estimating portion size was used in Malmo, Sweden. All dietary measurement instruments have been validated previously in a series of studies within the various source populations participating in EPIC.[20]

Daily intake of vitamin D, calcium, and magnesium was calculated by means of a standardized food composition data base across EPIC countries [21].

Demographic and lifestyle factors

To collect information on education, medical history (surgeries and previous illnesses), tobacco and alcohol consumption, and physical activity and other lifestyle factors, additional questionnaires were used. Height and weight were measured at baseline, except for the France and Oxford-UK study centre, where height and weight was self-reported.[18]

Ascertainment of type 2 diabetes

Ascertainment and verification of incident diabetes has been described in detail elsewhere.[19] In brief, incident cases were identified by self-reports (history of diabetes, physician-diagnosed diabetes, antidiabetic drug use), linkage to primary and secondary care registers, linkage to drug registers, hospital admissions and mortality data. Further verification of the diabetic cases came from individual medical record reviews.

Statistical analysis

Cox proportional hazard models adapted for case-cohort design according to the Prentice method were used to calculate hazard ratios (HR) and 95% confidence intervals (CI).[22] A Cox

model was used with stratification by age (in 1-year categories), centre and sex; Incident type 2 diabetes was the outcome variable and age was used as the underlying timescale.

Hazard ratios for dietary vitamin D intake are presented comparing quintiles taking the lowest quintile as reference. Quintile cutpoints were defined among subcohort members only. Different models were run to disentangle the effects of dietary vitamin D on type 2 diabetes: model 1: adjusted for total energy (kcal/day, cont.); model 2: adjusted for non-fat-energy (kcal/day, cont.), fat (g/day, cont., monounsaturated, polyunsaturated and saturated fat), physical activity (occupational, recreational and household activity; inactive, moderately inactive, moderately active, active, missing)[23], and model 3: as model 2 with further adjustment for a-priori defined potential confounders and risk factors for diabetes: BMI (kg/m^2, cont.), education level (none or primary school, technical/professional school, secondary school, longer education incl. university degree, unknown), smoking status (never, former, current, unknown), alcohol intake (g/day, cont.). Sensitivity analyses were performed excluding incident cases that occurred within the first two years of follow-up as well as additional adjustment for waist-hip-ratio.

In order to account for different levels of sunlight exposure, the EPIC centres were divided into 7 latitude group: below 42°N (Granada, Murcia, Ragusa, and Naples); 42°N - 44°N (Asturias, Navarra, San Sebastian, Florence, and South coast of France – centred in Marseille); 45°N - 46°N (Varese, Turin, and South of France – centred in Lyon); 47°N - 49°N (North-East and West of France – centred in Nantes and Paris, respectively – and Heidelberg); 50°N - 51°N (Potsdam, Utrecht, Bilthoven, Cambridge, and Oxford); 52°N - 56°N (Malmö, Aarhus, and Copenhagen); and above 57°N (Norway, and Umeå). A further sensitivity analysis was thus performed with additional adjustment for latitude.

Statistical interaction (heterogeneity) was evaluated with the Wald test by including cross-product terms of potential interaction variables (i.e., sex, physical activity, BMI) in the

179 respective models. Tests for trend over quintiles of intake (coded 1 to 5) were performed
180 using the Wald statistics.
181
182 To correct for measurement error, dietary intake data calculated from questionnaire data were
183 calibrated against 24 hour dietary recall data for a subsample (N = 2347). A fixed-effects
184 linear model was used in which centre and sex-specific recall data were regressed on the
185 dietary intakes.[24-26] The calibrated dietary data were used to model dietary intake of vitamin D
186 continuously in the whole sample and in the country-specific analysis. We used a meta-
187 analytic approach to investigate heterogeneity across centres (metan procedure in STATA) by
188 pooling the adjusted HR's per centre using the random effects model.
189 All tests were two-sided and considered to be statistically significant with a p-value of d0.05.
190 All analyses were conducted using SAS version 9.1 (SAS Institute, Cary, North Carolina) and
191 STATA version 10 for meta-analysis (College Station, Texas).
192
193 **Results**
194 Median vitamin D intake in the subcohorts of the respective countries by sex is shown in
195 Table 1. Dietary vitamin D intake was highest in Sweden and lowest in Italy. Vitamin D
196 intake was higher in men across all countries.
197 Median age at baseline was 52.7 years (IQR 46.5-59.2). The median follow-up time for the
198 study population was 10.8 years. Descriptive characteristics of the subcohort by quintiles of
199 vitamin D intake are shown in Table 2. The percentage of current smokers was lower in men
200 but higher in women with higher vitamin D intake. The increasing numbers of participants
201 with unknown physical activity with increasing vitamin D intake is due to physical activity
202 data not being collected in Umeå, Sweden, where vitamin D intake is high. No differences in
203 BMI were observed by quintiles of vitamin D intake. Total fish, meat, calcium and energy
204 intake was higher in both men and women with increasing vitamin D intake (table 2).

No significant association was observed between vitamin D intake and type 2 diabetes risk (Table 3). Hazard ratios (HR) and 95 % confidence intervals (CI) in the most adjusted model for the higher quintiles compared to the lowest were 1.04 (0.95-1.14), 1.02 (0.93-1.12), 1.06 (0.96-1.17) and 1.09 (0.97-1.22) (p-trend=0.17) (Table 3). We further performed a separate analysis by sex and did not find any significant association between diabetes incidence and vitamin D intake in either men or women ($p_{interaction}$ = 0.40). No statistical interaction was observed between BMI or physical activity groups and dietary vitamin D ($p_{interaction}$> 0.05). Moreover, there was no statistical interaction between vitamin D and calcium intake (p = 0.93).

To account for potential measurement error when calculating dietary intake from questionnaire data, we further performed an analysis using the continuous intake data calibrated with 24-hr dietary recall data from a subsample of the subcohort. The overall estimate showed no association for vitamin D and diabetes risk [HR (95% CI) =1.00 (0.97-1.03), per 1 µg/day increment] (Figure 1). The corresponding effect estimate using the observed (continuous) data was HR (95% CI) =1.03 (0.98-1.08). Country specific hazard ratios for the calibrated vitamin D intake (per 1 µg/day increment) in comparison with the overall effect estimate are shown in the forest plot (Figure 1). There was statistically significant heterogeneity across countries (I^2=60.9%, p = 0.012). Heterogeneity could in part be explained by the significant positive association in the UK data as exclusion of the UK data resulted in a non-significant and substantially decreased heterogeneity (I^2=18.6%, p = 0.228). In a sensitivity analysis, we excluded incident cases that occurred within the first two years of follow-up. No considerable changes in the hazard ratios were observed. We furthermore additionally adjusted for waist-hip-ratio and did not observe any changes in the effect estimates (waist-hip-ratio data are missing for the Umeå centre, n = 1796). As a proxy for sun exposure and thus endogenous vitamin D production we divided the centres in 7 categories according to their latitude. Adjustment for latitude did not notably change the

observed risk estimates for vitamin D and typ-2 diabetes risk. Furthermore, additional adjustment for calcium intake did not notably change the risk estimates.

Discussion

In this large prospective case-cohort analysis within the European Prospective Investigation into Cancer and Nutrition dietary vitamin D was not significantly associated with the incidence of type 2 diabetes. This was true for men and women. So far, only few cohort studies prospectively assessed the association between dietary vitamin D with the incidence of type 2 diabetes or diabetes related outcomes.[15-17] In line with our results, the Nurses' Health Study did not find a significant association between dietary or total intake of vitamin D and type 2 diabetes.[16] Furthermore, our results corroborate the findings from a large Japanese cohort that reported no association in men or in women.[17] However, the Women's Health Study reported an inverse association between dietary vitamin D intake and the prevalence of metabolic syndrome[15], and also a meta-analysis of these three studies found a borderline inverse association between vitamin D intake >500 U/d (>12.5 µg/d) and type 2 diabetes incidence.[11]

Systematic reviews focusing on eight randomized trials did also not provide clear evidence for an inverse association of vitamin D supplementation with hyperglycemia or incident type 2 diabetes.[11] The so far largest trial, the Women's Health Initiative (WHI) study, did not observe any risk reduction of type 2 diabetes over 7 years of follow-up in the intervention arm with supplementation of vitamin D (400 IU/d) and calcium (1000 mg/d).[27] However, the authors noted, that higher doses of vitamin D may have been necessary to affect diabetes risk.

Several explanations are possible as to why we did not observe any association between dietary vitamin D and type 2 diabetes risk in our study: 1) there is indeed no relationship; 2) the amount and variation of dietary vitamin D intake is too low in the population to detect potential effects; especially, dietary vitamin D intake is distinctly lower in most European

257 countries as compared to the US where staple food is frequently fortified with vitamin D, and
258 thus dietary vitamin D intake more effectively impacts on the overall vitamin D status of a
259 person.
260 The present study is thus far the largest study prospectively assessing the association between
261 dietary vitamin D intake and the risk of type 2 diabetes. Thus, power was high to detect even
262 weak associations. Further strengths of the study were the high quality of physician-verified
263 diagnoses of type 2 diabetes; the calibration of nutrient intake data from questionnaires with
264 that from 24 h recall data; and the inclusion of detailed information on potential confounders
265 in the analysis. However, due to the observational study design, residual confounding cannot
266 completely be ruled out. A further strength of the study is the wide range of intake from
267 different European countries with different eating habits. The intake data in our study was
268 comparable to that in representative studies in Europe.[28-30] Particularly, the here presented
269 higher intake in the northern European countries, e.g. Sweden, where intake of vitamin D-rich
270 foods and the contribution from fortified foods is high, is in line with previous reports.[28,31]
271 There are, however, several limitations that should be noted when interpreting the results.
272 Firstly, we did not account for vitamin D from supplements. Additional adjustment on
273 unspecified supplement intake in the study population did not change the risk estimates, but
274 calculated amounts of vitamin D from supplements were not available. Secondly, the
275 contribution of endogenous production of vitamin D (following UVB exposure) could not be
276 addressed here. In a sensitivity analysis, we adjusted for centers' latitude as a proxy for sun
277 exposure, which did not affect the risk estimates. However, since the contribution of diet to
278 the overall vitamin D status of a person is low, studies with information on the entire vitamin
279 D status may lead to a different conclusion. Indeed, prospective observational studies with
280 serum 25(OH)D measurements showed a strong inverse association between vitamin D status
281 and type 2 diabetes.[10-13] However, these studies can also be subject to substantial residual

confounding, e.g. by imprecise assessment of outdoor physical activities which are correlated with both UVB exposure and, eventually, with vitamin D status as well as with diabetes risk. In summary, in the present study we did not observe an association between dietary vitamin D intake and the risk of type 2 diabetes in a large European study population. However, it has to be acknowledged that endogenous production of vitamin D in the skin following UVB exposure is the dominant predictor of vitamin D status in humans.

Acknowledgements

We thank all EPIC participants and staff for their contribution to the study. We thank Nicola Kerrison (MRC Epidemiology Unit, Cambridge) for managing the data for the InterAct project. We further thank Valentina Gallo (Imperial College London) for providing information on dividing the EPIC centres into latitude groups. Funding for the InterAct project was provided by the EU FP6 programme (grant number LSHM_CT_2006_037197). In addition, InterAct investigators acknowledge funding from the following agencies: E Ardanaz: Health Research Fund (FIS) of the Spanish Ministry of Health and Navarre Regional Government; JWJ Beulens: Verification of diabetes cases in EPIC-NL was additionally funded by NL Agency grant IGE05012 and an Incentive Grant from the Board of the UMC Utrecht; PW Franks: Swedish Research Council, Novo Nordisk, Swedish Diabetes Association, Swedish Heart-Lung Foundation; R Kaaks: German Cancer Aid, German Ministry of Research (BMBF); TJ Key: Cancer Research UK; KT Khaw: Medical Research Council UK, Cancer Research UK; T Kühn: German Cancer Aid; P Nilsson: Swedish Research Council; K Overvad: Danish Cancer Society; JR Quirós: Asturias Regional Government; O Rolandsson: The Västerboten County Council; I Sluijs: Verification of diabetes cases was additionally funded by NL Agency grant IGE05012 and an Incentive Grant from the Board of the UMC Utrecht; AMW Spijkerman: Dutch Ministry of Public Health, Welfare and Sports (VWS), Netherlands Cancer Registry (NKR), LK Research

Funds, Dutch Prevention Funds, Dutch ZON (Zorg Onderzoek Nederland), World Cancer Research Fund (WCRF), Statistics Netherlands; A Tjonneland: Danish Cancer Society; R Tumino: AIRE-ONLUS Ragusa, AVIS-Ragusa, Sicilian Regional Government; DL van der A: Dutch Ministry of Public Health, Welfare and Sports (VWS), Netherlands Cancer Registry (NKR), LK Research Funds, Dutch Prevention Funds, Dutch ZON (Zorg Onderzoek Nederland), World Cancer Research Fund (WCRF), Statistics Netherlands; R Zamora-Ros: the Health Research Fund (FIS) of the Spanish Ministry of Health (RTICC DR06/0020/0091); E Riboli: Imperial College Biomedical Research Centre.

Conflict of interest

None declared.

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TABLE 1 Dietary vitamin D intake by sex and country in the subcohort[1]: the EPIC-InterAct study

Country	Men		Women	
	Median	IQR	Median	IQR
All	3.6	1.6-7.7	2.4	1.1-4.6
France	--	--	1.3	0.7-2.5
Italy	1.3	0.8-2.7	1.0	0.5-2.1
Spain	2.7	1.3-8.7	1.7	0.9-4.4
UK	3.5	1.7-5.2	2.4	1.7-3.8
Netherlands	3.4	2.3-7.4	2.5	1.8-3.9
Germany	2.0	1.1-3.6	1.5	0.8-3.3
Sweden	7.1	4.5-9.6	4.7	3.3-6.7
Denmark	2.9	1.4-7.7	1.7	1.0-3.9

[1] Vitamin D intake in µg/day from 24-hour recall data (N =2347); IQR, inter-quartile range

TABLE 2 Baseline characteristics in the subcohort by sex and quintiles of dietary vitamin D intake: the EPIC-InterAct study

Vitamin D (µg/day)	Quintile 1 < 2.19 (Median: 1.6)		Quintile 2 2.19-<3.13 (Median: 2.6)		Quintile 3 3.13-<4.27 (Median: 3.7)		Quintile 4 4.27-<6.07 (Median: 5.0)		Quintile 5 e 6.07 (Median: 7.9)	
Men	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
	N = 744		**N = 903**		**N = 1109**		**N = 1418**		**N = 1794**	
Smoking status										
Never	201	27	275	30	353	32	461	33	591	33
Former	278	37	349	39	402	36	515	36	627	35
Current	259	35	269	30	333	30	430	30	567	32
Unknown	6	1	10	1	21	2	12	1	9	1
Education										
Primary school or less	348	47	335	37	413	37	502	35	731	42
Technical/professional school	140	19	200	22	260	23	351	25	388	22
Other secondary education	92	12	133	15	132	12	160	11	260	14
University	154	21	220	24	281	25	385	27	398	22
Unknown	10	1	15	2	23	2	20	1	17	1
Physical activity										
Inactive	201	27	258	29	284	26	374	26	348	19
Moderately inactive	243	33	274	30	339	31	397	28	603	34
Moderately active	224	30	261	29	314	28	359	25	474	26

Active	60	8	79	9	91	8	114	8	108	6
Unknown	16	2	31	3	81	7	174	12	261	15

	Median	**IQR**	**Median**	**IQR**	**Median**	**IQR**	**Median**	**IQR**	**Median**	**IQR**
Age at recruitment	52.7	46.3-58.4	52.8	45.9-58.5	52.9	46.5- 58.6	53.0	47.3- 59.6	53.8	48.6- 60.3
BMI (kg/m2)	26.7	24.5-28.9	26.4	24.1-28.8	26.2	24.2-28.6	26.3	24.5-28.7	26.2	24.0-28.7
Total energy (Kcal/d)	2048	1685-2457	2256	1860-2713	2330	1963-2736	2443	2052-2869	2678	2273-3150
Saturated fat (g/d)	24.5	18.6-31.0	30.1	23.4-37.4	32.2	24.9-40.8	34.8	27.0-43.5	41.2	31.8-52.4
Monounsaturated fat (g/d)	28.3	21.0-38.9	31.5	23.0-41.9	31.5	24.3-42.0	33.6	26.5-42.7	39.2	31.6-48.7
Polyunsaturated fat (g/d)	9.9	7.6-13.6	11.6	9.2-15.3	13.2	10.4-16.8	14.0	10.9-18.4	16.7	13.2-21.7
Alcohol (g/d)	13.5	3.1-34.0	16.3	5.4-38.4	16.4	5.2-37.3	14.8	4.9-37.8	13.2	4.1-31.0
Calcium (mg/d)	804	595-1047	885	669-1173	931	720-1233	968	735-1261	1109	836-1400
Magnesium (g/d)	335	267-410	351	295-421	369	312-438	391	323-458	412	347-483
Coffee (g/d)	120	56-413	175	65-500	287	90-600	385	131-665	400	145-675
Soft drinks (g/d)	0.0	0.0-39.4	6.7	0.0-66.7	8.1	0.0-85.7	16.4	0.0-97.5	21.3	0.0-114
Total meat (g/d)	101	66-146	119	86-159	130	91-170	134	98-178	142	102-193
Total fish (g/d)	10.0	3.1-22.4	16.4	8.2-28.4	22.7	12.7-36.3	29.4	15.3-47.6	37.7	15.4-67.7

Vitamin D (µg/day)	Quintile 1 < 2.19 (Median: 1.6)		Quintile 2 2.19-<3.13 (Median: 2.6)		Quintile 3 3.13-<4.27 (Median: 3.7)		Quintile 4 4.27-<6.07 (Median: 5.0)		Quintile 5 e 6.07 (Median: 7.9)	
Women	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
	N = 2415		**N = 2257**		**N = 2050**		**N = 1742**		**N = 1366**	
Smoking status										
Never	1416	59	1244	55	1143	56	963	55	694	51
Former	482	20	523	23	440	21	350	20	296	22
Current	494	20	476	21	447	22	408	23	367	27
Unknown	23	1	14	1	20	1	21	1	9	1
Education										
Primary school or less	1077	45	916	41	780	38	672	39	571	42
Technical/professional school	443	18	499	22	508	25	447	26	366	27
Other secondary education	438	18	393	17	363	18	249	14	157	11
University	420	17	408	18	356	17	339	19	255	19
Unknown	37	2	41	2	43	2	35	2	17	1
Physical activity										
Inactive	274	11	263	12	248	12	197	11	151	11
Moderately inactive	611	25	551	24	466	23	435	25	418	31
Moderately active	1237	51	1111	49	951	46	769	44	588	43

Active	244	10	238	11	214	10	156	9	102	7
unknown	49	2	94	4	171	8	185	11	107	8
	Median	**IQR**	**Median**	**IQR**	**Median**	**IQR**	**Median**	**IQR**	**Median**	**IQR**
Age at recruitment	52.3	45.3-58.8	52.4	46.3-58.7	51.9	46.0-58.5	52.1	46.1-59.3	53.3	47.1-61.0
BMI (kg/m2)	24.9	22.4-28.3	24.9	22.5-27.9	25.0	22.6-28.1	24.7	22.5-28.0	25.0	22.6-28.2
Total energy (Kcal/d)	1625	1353-1926	1836	1529-2185	1916	1604-2282	2001	1695-2404	2185	1861-2563
Saturated fat (g/d)	22.1	16.5-27.8	27.0	21.1-34.0	28.5	21.8-36.3	30.7	24.1-39.0	35.2	26.7-44.0
Monounsaturated fat (g/d)	22.3	16.3-30.5	25.4	19.1-33.8	26.4	20.5-35.0	27.8	22.4-35.8	32.3	26.3-40.2
Polyunsaturated fat (g/d)	8.8	6.8-11.4	10.7	8.4-14.0	11.5	8.9-14.7	12.3	9.4-16.4	14.2	11.3-18.2
Alcohol (g/d)	1.9	0.0-10.1	3.0	0.3-11.6	3.7	0.4-11.6	4.0	0.6-12.1	5.0	0.7-12.8
Calcium (mg/d)	806	614-1033	904	711-1147	957	727-1212	995	770-1244	1062	861-1326
Magnesium (g/d)	283	233-343	309	257-369	327	275-386	337	283-404	348	300-408
Coffee (g/d)	150	58-437	250	84-500	290	100-523	330	129-582	375	150-600
Soft drinks (g/d)	0.0	0.0-36.2	0.0	0.0-46.2	3.3	0.0-55.7	6.5	0.0-85.7	6.0	0.0-85.7
Total meat (g/d)	75	47-106	91	62-120	94	65-129	95	68-126	99	71-131
Total fish (g/d)	9.5	3.2-21.5	16.1	7.0-29.7	22.7	9.8-36.0	27.2	11.2-46.3	37.8	17.4-66.2

N = 15798; IQR: inter-quartile range

TABLE 3 Dietary vitamin D intake and risk of type 2 diabetes: the EPIC-InterAct study

	Model 1[1]		Model 2[1]		Model 3[1]	
Quintiles of vitamin D intake (µg/day)	HR	95% CI	HR	95% CI	HR	95% CI
< 2.19	Ref.		Ref.		Ref.	
2.19-<3.13	1.04	(0.96 - 1.13)	1.02	(0.94- 1.11)	1.04	(0.95- 1.14)
3.13-<4.27	1.02	(0.94 - 1.11)	1.00	(0.91- 1.08)	1.02	(0.93- 1.12)
4.27-<6.07	1.09	(1.00 - 1.19)	1.05	(0.96- 1.15)	1.06	(0.96- 1.17)
e6.07	1.18	(1.06 - 1.30)	1.10	(0.99- 1.22)	1.09	(0.97- 1.22)
p-trend	0.002		0.078		0.170	

[1] All models stratified by sex, age and study centre; model 1: adjustment for total energy; model 2: adjustment for non-fat energy, polyunsaturated fatty acids, monounsaturated fatty acids, saturated fatty acids, physical activity; model 3: as model 2 with further adjustment for education, BMI, smoking, alcohol intake; HR = hazard ratio, CI = confidence interval.

FIGURE 1 Dietary vitamin D intake (per 1 µg/day) and risk of type 2 diabetes, by country and overall: the EPIC-InterAct study; CI = confidence interval.

(Models stratified by sex and age; adjusted for non-fat energy, polyunsaturated fatty acids, monounsaturated fatty acids, saturated fatty acids, physical activity, education, BMI, smoking, alcohol intake.)